LABELING

5.1

CRYOCATH

7F Freezor®
Cardiac Cryoablation Catheter

Instructions For Use

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Manufacturer:	Authorized representatives:	
	United States of America	**Europe**
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Device Description

The 7F Freezor® Cardiac Cryoablation Catheter and CCT 2 CryoConsole System consists of a CryoConsole, the Freezor® Catheter, connection components and accessories

The Freezor® Catheter is a flexible, steerable device specifically designed for tissue cryomapping and cryoablation Electrodes at the tip surface provide temperature-reading capabilities. Freezor® Catheters are introduced into the vasculature by traditional minimally invasive techniques. The distal end of the Freezor® Catheter reaches temperatures as cold as -75°C when refrigerant is injected from the console to the tip of the catheter.

Indications for Use

The 7F Freezor® Cardiac Cryoablation Catheter and CCT.2 CryoConsole System and related accessories are indicated for the cryoablation of the conducting tissues of the heart in the treatment of patients with atrioventricular nodal reentrant tachycardia (AVNRT).

Contraindications

This device is contraindicated:

- In patients with active systemic infection.
- In conditions where manipulation of the catheter would be unsafe (e.g. intracardiac mural thrombus).
- In patients with cryoglobulinemia

Warnings

- Additional studies are needed to fully characterize the impact of cryomapping with respect to patient outcomes.
- The Freezor® Catheter contains pressurized refrigerant during operation. Release of this gas into the circulatory system due to equipment failure or misuse could result in gas embolism.
- If an unanticipated event occurs, stop the procedure at any time by pushing the RED button on the console control panel.
- Do not pull on the Freezor® Catheter, umbilicals or CryoConsole while the catheter tip is frozen to the endocardial tissue, as this could lead to cardiac or vascular damage.
- Do not connect the Freezor® Catheter to any radio frequency generator or use the Freezor® Catheter to deliver RF ablation energy, because this could cause catheter malfunction and / or patient harm.
- Introducing any catheter into the circulatory system entails the risk of gas embolism, which can occlude vessels and lead to tissue infarction with serious consequences.
- Catheter procedures may mechanically induce arrhythmias.
- The use of fluoroscopy during catheter ablation procedures presents the potential for significant x-ray exposure to both patients and laboratory staff. Extensive exposure can result in acute radiation injury and increased risk for somatic and genetic effects. Only perform catheter ablation after giving adequate attention to the potential radiation exposure associated with the procedure, and taking steps to minimize this exposure. Give careful consideration before using the device in pregnant women.
- Careful catheter manipulation must be performed in order to avoid cardiac damage such as perforation or tamponade.
- Catheter advancement should be performed under fluoroscopic guidance. Do not use excessive force to advance or withdraw the Freezor® Catheter, especially if resistance is encountered. Ensure the appropriate intravascular tip positioning
- Catheter entrapment within the heart or blood vessels is a possible complication of cardiac ablation procedures. The potential for catheter entrapment may be increased when the catheter is

positioned in the vicinity of the chordae tendinae The occurrence of this complication may necessitate surgical intervention and/or repair of injured tissues

- Do not pass the catheter through any prosthetic heart valve (mechanical or tissue), as this may cause entrapment of the catheter and/or damage to the prosthetic heart valve, resulting in valvular insufficiency and/or premature failure of the prosthetic valve

Precautions

- Do not re-sterilize or re-use any Freezor® Catheter or sterile accessory under any circumstances Freezor® Catheters and sterile accessories are designed for single use only
- Discard all used Freezor® Catheters and sterile accessories in accordance with hospital procedures.
- Ensure that equipment used with the Freezor® Catheters and CryoConsole is electrically safe and does not expose the patient to hazards.
- Use only Freezor® Catheters, accessories and refrigerant tanks that have been obtained from CryoCath Technologies Inc. with the CryoConsole.
- Consider peri-procedural anticoagulation therapy for patients undergoing right-sided procedures. Administer anticoagulation therapy, if performed, before and after the procedure according to the institution's standards.
- Prior to removing the Freezor® Catheter or the accessories from their respective packaging, inspect the packaging to verify the integrity of the seal. Use sterile techniques when handling the product.
- Do not preshape or bend the Freezor® Catheter shaft or tip at any time. Excessive bending or kinking of the Freezor® Catheter shaft may damage internal structures and increase the risk of catheter failure. Preshaping of the distal curve can damage the steering mechanism.
- Do not use the Freezor® Catheter if it is kinked or damaged. If the Freezor® Catheter becomes kinked or damaged while in the patient, remove it and use a new catheter. Prior to injecting, the physician should ensure that there is no kink in the Freezor® Catheter.
- Only appropriately trained personnel in a fully equipped electrophysiology laboratory should perform cardiac cryoablation procedures.
- Do not expose the Freezor® Catheter handle, sterile accessories, and electrical connectors to fluids or solvents.
- If patients need to be defibrillated during the procedure, disconnect the Freezor® Catheter's electrical connection prior to defibrillation.
- Position the Freezor® Catheter to ensure good tip contact prior to injection of refrigerant..
- Use adequate filtering on the recording system to allow continuous monitoring of the surface electrocardiogram (ECG) during cryoapplications.
- Use an appropriate introducer with the Freezor® Catheter. Please refer to the appendix for the chosen catheter to determine the correct size introducer to use.
- Always pull the thumb knob to straighten the Freezor® Catheter tip before insertion or withdrawal of the catheter.
- The CryoConsole meets the requirements of IEC601-1 (UL Report 75HN). It is the user's responsibility after installation to verify and ensure that the CryoConsole meets the applicable electrical safety requirements.

Potential Adverse Events

Adverse events that may be associated with cardiac catheterization and ablation listed alphabetically below include but are not limited to:

Access site complications including pain, hematoma, ecchymosis, infection, thrombosis or AV fistula; arrhythmias include new arrhythmias and / or worsening of existing arrhythmias; cardiac arrest and / or death, cardiac perforation with hemopericardium and/or tamponade; catheter entrapment in cardiac structures requiring surgical intervention; chest pain; coronary artery spasm / dissection / thrombosis; endocarditis; exposure to X ray energy with possible cancer risk or harm to

fetus, gas embolism with possible tissue infarction, heart block, partial or complete, potentially requiring implantation of a permanent pacemaker, hemorrhage, hemothorax, myocardial infarction; pericardial effusion, pericarditis or pericardial effusion, pleural effusion, pneumothorax; pseudoaneurysm; pulmonary edema; pulmonary embolism; stroke, thrombus, intravascular or intracardiac; thromboembolism with potential tissue infarction; transient ischemic attack, valvular damage, vasovagal reaction

Clinical Studies

Summary of Clinical Studies

Study Design

The Freezor® Catheter and CryoConsole System was evaluated in a clinical study for the treatment of supraventricular tachycardias (SVT). The study was designed as a nonrandomized, single-arm, multicenter study to assess the safety and effectiveness of the device used percutaneously in the treatment of AVNRT, AVRT and refractory AF in subjects acting as their own controls.

Study Endpoints

The endpoints for the study were as follows:

- major complications - defined by the absence of serious complications associated with the use of the investigational device within seven days of the ablation procedure;
- acute success - defined as the absence of recurrence and non-inducibility of sustained SVT at the end of the procedure;
- chronic success - defined as no recurrence of sustained SVT at three months post-ablation.

Safety was analyzed for each arrhythmia group (i.e., AVNRT, AVRT, AF) and overall by calculating the proportion and exact two-sided 95% confidence intervals for acute major complications.

After treatment, the subjects remained hospitalized per hospital procedure under continuous electrocardiogram monitoring, and post procedure assessments were performed. Subsequent follow-up was scheduled at 1 week (telephone interview), at 1 and 3 months (clinic visits) and at 6 months (telephone interview) after the procedure.

Description of Subjects

A total of 166 subjects were enrolled in the study. Of the 166 enrolled subjects, final diagnoses were AVNRT, 102 (61%); AVRT, 51 (31%); AF, 12 (7%); and 1 subject with a non-protocol arrhythmia [atrial tachycardia (AT)], who was initially misdiagnosed with AVNRT (this patient is categorized in the AVNRT in the analyses described below). Of the 166 enrolled subjects, 164 were treated with cryoablation and constitute the intent-to-treat (ITT) population. Two patients did not receive cryoablation due to equipment problems.

Demographics

The study population consisted of 53 (32%) men and 113 (68%) women Patient demographics for the study are shown in the table below

Table 1: Summary of Demographic Data of Enrolled Subjects (n=166)

Diagnosis	Number of Subjects	Age (yr)	Sex n (%)
AVNRT	103	50 ± 15	M. 31 (30) F: 72 (70)
AVRT	51	39 ± 13	M: 18 (35) F: 33 (65)

AF	12	73 ± 11	M: 4 (33) F 8 (67)
Overall	166	48 ± 16	M: 53 (32) F 113 (68)

AF, atrial fibrillation, AVRT, atrioventricular reentrant tachycardia;

Cryoablation Procedure Data

The treatment of AVNRT utilizing the Freezor® Catheter was attempted by using the cryomapping function prior to cryoablation of the targeted substrate or by proceeding directly with the ablation of the targeted substrate without cryomapping The table below describes the cryoablation procedural information

Table 2: Cryoablation Procedure Data

Parameter	Mean ± SD (Range)	Subjects (n)
Cryoablation attempts	1230 times	164
Cryoablation attempts/patient	7.5 ± 6.6 (1 – 36)	164
Fluoroscopy duration (min)	24.9 ± 24.0 (1 – 115)	162
Total EPS procedure duration (min)	265 2 ± 120.8 (115 – 920)	164

Safety Results

The safety of the device was evaluated via an assessment of the acute major complication rate and compared to the goal of the objective performance criteria for safety. Eight (8) acute major complications (AMCs) were reported in 7/166 patients (4.2%, upper bound 8.5%). The clinical study safety results exceeded the safety objective performance criteria of 2.5% with an upper bound of 7.0%

Eighty-seven (52%) of the 166 safety subjects evaluated in this study reported one or more AEs. Device-related AEs were reported for 11 (7%) of the 166 enrolled subjects. The table below summarizes this information per patient arrhythmia type:

Table 3: Subjects with Adverse Events (n=166)

Adverse Event Type	AVNRT (n = 103)	AVRT (n = 51)	AF (n = 12)	All subjects (n = 166)
	n (%)	n (%)	n (%)	n (%)
adverse event	52 (50)	29 (57)	6 (50)	87 (52)
serious adverse event	8 (8)	6 (12)	6 (50)	20 (12)
acute major complication	3 (3)	4 (8)	0 (0)	7 (4 2)
death	0 (0)	0 (0)	1 (8)	1 (0 6)

The AMCs consisted of pulmonary embolism, prostatitis secondary to Foley catheter placement, thrombus in IVC after cryoablation and RF ablation, subtotal RCA occlusion with MI in a patient after failed cryoablation and RF ablation of left sided pathway, sheared introducer for diagnostic catheter, pericardial perforation by diagnostic catheter requiring pericardiocentesis, deep venous thrombophlebitis, and thrombus formation on diagnostic catheter requiring removal of catheter. One patient died 4 months post-procedure This death was not considered related to the study device or procedure

Effectiveness Results: Acute Success and Chronic Success

The table below summarizes the acute success and chronic success in the ITT patient population for the AVNRT group

Table 4: Acute Success and Chronic Success (ITT) for AVNRT Group

Diagnosis	N	Acute Procedural Success N (%, lower bound CI %)	Long Term Clinical Success* % (lower bound CI %)
AVNRT	103	94 (91, 82)	93% (85)*

*Bonferroni adjusted confidence interval

10.7 Cryomapping

One AVNRT subject had a cryomapping related adverse event (transient AV block lasting 25 seconds which resolved completely without treatment). The table below summarizes the cryomapping-related adverse events.

Table 5: Summary Data for Cryomapping-Related Adverse Events (ITT Subjects; n=164)

Diagnosis	ITT Subjects who had Cryomapping Attempts* n (%)	ITT Subjects with Cryomapping- related AEs n (%)
AVNRT #	86 / 102 (84%)	1 / 86 (1.1%)
AVRT	38 / 49 (78%)	0 / 38 (0%)
AF	10 / 12 (83%)	0 / 10 (0%)
AT	1 / 1 (100%)	0 / 1 (0%)
Overall	135 / 164 (82%)	1 /135 (0.7%)

\# Excluding subject 0915 with AT
* The number of intent-to-treat subjects who had one or more cryomapping attempts.

How Supplied

The Freezor® Catheter, coaxial umbilical, and electrical umbilical are supplied sterile and packaged individually.

How to Connect

Refer to the CryoConsole Operator's Manual for detailed instructions.

1. Connect the Freezor® Catheter to a sterile coaxial umbilical and a sterile electrical umbilical.
2. Connect the coaxial umbilical to the CryoConsole and the electrical umbilical to the ECG connection box.

Directions for Use

IMPORTANT: Refer to the CryoConsole Operator's Manual for detailed instructions.

Refer to the Warnings and Precautions at the beginning of this document.

1. All mapping and ablation procedures must be performed in a fully equipped electrophysiology laboratory
2. Prior to introducing the Freezor® Catheter into the patient, test the deflection mechanism by pulling back on the knob on the handle to ensure that it is operational.
3. Using aseptic technique, create a vascular access with an 8F introducer, and insert the Freezor® Catheter.
4. Under fluoroscopic guidance, position the tip of the Freezor® Catheter at the desired endocardial site for cryomapping or cryoablation

5 The Freezor® Catheter tip can be deflected to facilitate positioning by using the thumb knob to vary tip curvature Pushing the thumb knob forward causes the Freezor® Catheter tip to bend, pulling the knob back causes the tip to straighten

6 Two energy delivery modes can be utilized: cryomapping or cryoablation. Cryomapping is a feature that uses warmer temperatures and shorter duration time to reversibly assess the target ablation area The preset parameters for cryomapping are a temperature of –30°C and a duration of 60 seconds

7. Because of the complexity of arrhythmia electrophysiology, four (4) different cryomapping techniques may be used to assess catheter tip position in AVNRT subjects:

- change in the slow pathway ERP
- change in the maximal AH interval during pacing
- termination of the target arrhythmia
- uninducibility of the target arrhythmia.

8. In the cryoablation mode, the preset (and coldest) temperature available is –75°C. The preset duration is 240 seconds Effective ablation of the desired cardiac tissue can be demonstrated by assessing the inducibility of the target arrhythmia after cryoablation has been completed.

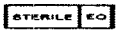
Physician training

1. Physicians must be familiar with the techniques and appropriately trained for cardiac mapping and ablation procedures.

2. Physicians must have received an in-service from qualified CryoCath Technologies personnel regarding the 7F Freezor® Cardiac Cryoablation Catheter and CCT.2 CryoConsole System prior to performing the initial case with the system.

3 CryoCath Technologies personnel must be present during the first two procedures performed with the system to answer any technical questions regarding the system. .

SYMBOL: Catheter label:

Symbol	Definition
	Expiration date
	Lot number
REF	Reference number
	Method of sterilization ethylene oxide
	Single-use
	Attention, See instructions for Use
	Fragile
	Protect from elements

	This side Up
	Store above 0°C/32°F
	Recycled